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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,399	07/01/2003	John R. Desjarlais	67461-5097US01	1891

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EXAMINER

EMCH, GREGORY S

ART UNIT	PAPER NUMBER
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1649

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/611,399	DESJARLAIS ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 October 2006 and 03 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17,18,20,22-26 and 36-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17,18,20,22-26 and 36-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02/06/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

Claims 17, 18 and 36-42 have been amended, claims 19, 21 and 33 have been canceled and new claim 45 has been added as requested in the amendment filed on 18 October 2006. Following the amendment, claims 17, 18, 20, 22-26 and 36-45 are pending in the instant application.

Claims 17, 18, 20, 22-26 and 36-45 are under examination in the instant office action.

The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

Information Disclosure Statement

A signed and initialed copy of the IDS paper filed 06 February 2007 is enclosed in this action.

Double Patenting

The provisional obviousness-type double patenting rejection of claims 18, 23-26 and 36-44 as being unpatentable over claims 1-16 of copending application No. 10/963,994 is maintained for reasons of record and as set forth below. Furthermore,

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claims 17, 20, 22 and newly added claim 45 are subject to the instant provisional rejection.

The provisional obviousness-type double patenting rejection of claims 17, 18, 24 and 36-43 as being unpatentable over claims 1-16 of copending application No. 11/008,091 is maintained for reasons of record and as set forth below. Furthermore, claims 20, 22, 23, 25, 26 and 44 and newly added claim 45 are subject to the instant provisional rejection.

In the reply filed 18 October 2006, Applicants request that the instant rejection be held in abeyance until allowable subject matter has been found in the instant application or in the instant co-pending applications. However, until such a time occurs, the rejections are maintained.

Additionally, claims 17, 18, 20, 22-26 and 36-45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18, 23-26, 33, 36, 37, 39-41, 43 and 44 of copending application No. 10/338,083. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '083 application are drawn to variant TNFSF variant monomers and oligomers with the same functional properties as in the instant claims, i.e., reduced receptor activation when compared to naturally occurring TNFSF proteins. Furthermore, the claims of the '083 application recite the same amino acid substitutions to TNF- α as those recited by the instant claims.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 17, 18, 20, 22-26 and 36-45 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 7,101,974. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '974 patent are drawn to variant TNFSF variant monomers and oligomers with the same functional properties as in the instant claims, i.e., reduced receptor activation when compared to naturally occurring TNFSF proteins. Furthermore, the claims of the '974 patent application recites the same amino acid substitutions to TNF- α as those recited by the instant claims.

It is noted that the instant rejection was set forth in the previous office action as a provisional rejection over application number 09/981,289. Said application has since issued as the '974 patent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

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only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 17, 18, 20, 22-25 and 36-45 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,171,787 to Wiley.

In the reply filed 18 October 2006, Applicants assert that the '787 patent does not anticipate the present claims as amended because the '787 patent discloses a naturally occurring TNFSF protein with non-conservative mismatches. Applicants also assert that nowhere does the '787 patent disclose that a non-naturally occurring TNFSF having at least a 90% decrease in receptor activation as compared to a naturally occurring TNFSF oligomer. Applicants further submit that the '787 patent only discloses purified, naturally occurring TNFSF proteins, whereas claim 17 claims a mixed TNFSF oligomer comprising at least one non-naturally occurring variant TNFSF protein having at least a 50% decrease in receptor activation as compared to a homotrimer of a naturally occurring TNFSF protein. In addition, Applicants assert that the '787 patent does not teach making at least one amino acid substitution in the Large Domain and at least one amino acid substitution in a domain selected from the group consisting of the DE Loop and the Small Domain.

Applicants' arguments have been fully considered and are not found persuasive. Although the patent teaches a naturally occurring protein, it also teaches non-naturally occurring proteins. For example, the patent teaches "an engineered soluble version of TNF-gamma, as well as cell surface expressed form of TNF-gamma" (col.2, lines 12-14), recombinant polypeptides (col.11, lines 1-11) and "synthetic peptides" (co.11, lines

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12-15). Furthermore, although the Wiley patent does not appreciate the claimed functions of the encoded polypeptides, these would nonetheless be inherent properties of the polypeptides. Applicants are reminded that chemical compounds and their properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA1963)), as are their processes and yields (*In re Von Schickh*, 362 F.2d 821, 150 USPQ 300 (CCPA 1966)). Thus, absent evidence to the contrary, the Wiley patent inherently teaches the functions of the polypeptides of the instant claims.

Therefore, the '787 patent discloses a TNFSF protein that is 28.7% homologous with Applicant's SEQ ID NO: 8, with non-conservative mismatches at, for example, positions 29, 34, 84, 91, and 97, thus meeting the limitations of claims of 18, 24, 36, and 38-43. The '787 patent teaches that approximately the first 150 N-terminal amino acids are located in the receptor contact position (col.1, lines 52-61). Thus, since the mismatches recited *supra* occur within these residues as well as within the trimer interface domain, and since substitutions in the receptor contact region and the trimer interface domain would encompass surface substitutions, claims 23, 37 and 38 are anticipated. Furthermore, the '787 patent discloses pharmaceutical compositions for administration in a subject, thus meeting the limitations of claim 45 (col. 8, lines 30-37; col.30, lines 6-19).

The '787 patent also discloses TNFSF proteins (col.40, lines 17-28), variants of said proteins (col.40, lines 29-46), and oligomers, trimers, dimers and higher order oligomers of said TNFSF proteins and variants (col.40, lines 47-52), thus meeting the limitations of claims 17, 22, and 25. Furthermore, the '787 patent discloses synthetic

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fragments with or without substitutions, which inhibit activation of the TNFSF polypeptide or the TNFSF receptor and discloses that said polypeptide can be a soluble fragment, which is capable of binding a receptor for TNF-gamma (col.4, lines 31-39; col.31, line 66 – col.32, line 21). Thus, since inhibitors that bind to soluble TNFSF polypeptides that normally bind to a TNFSF receptor are contemplated, the limitations of claims 20 and 44 have been met.

Since the patent discloses all the elements of the claims, claims 17, 18, 20, 22-25 and 36-45 are anticipated by U.S. Patent No. 6,171,787 to Wiley.

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

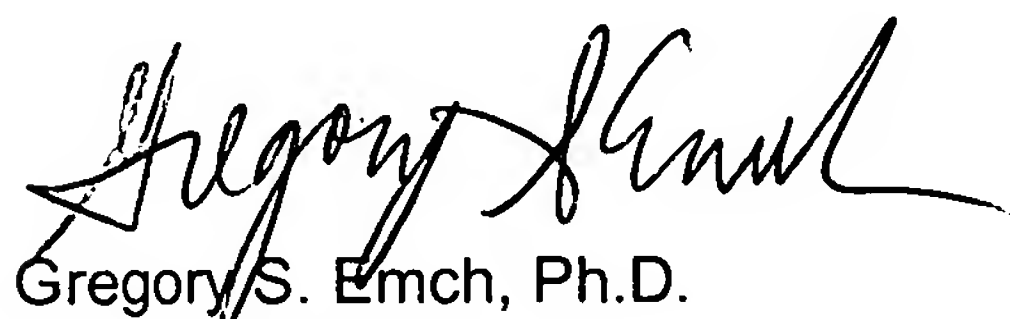
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Advisory Information

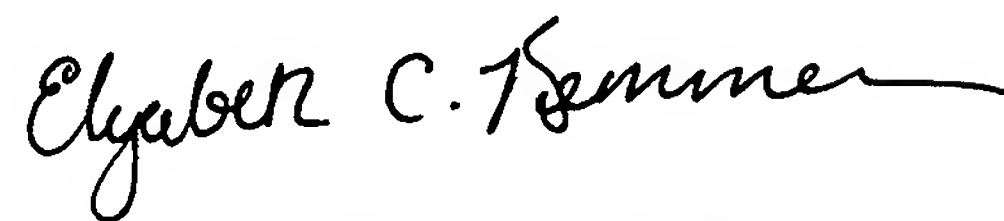
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is 571-272-8149. The examiner can normally be reached Monday through Friday from 9:00AM to 5:30PM (EST) .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
09 March 2007



ELIZABETH KEMMERER
PRIMARY EXAMINER